THE EFFECT OF EXERCISE ON THE RENAL PLASMA FLOW AND FILTRATION RATE OF NORMAL AND CARDIAC SUBJECTS[1]

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In a previous communication (1) evidence was presented for a "forward failure" hypothesis of edema in patients who have low cardiac outputs at rest. These patients have a low renal blood flow, apparently accompanied by renal efferent arteriolar constriction. This seems to be directly related to the level of the cardiac output and is entirely unrelated to the height of the venous pressure. As the renal blood flow falls, a consequent reduction in filtration rate occurs. This results in a decrease in the amount of salt and water filtered, and, since the tubules continue to reabsorb salt and water almost completely, there is a net retention of the latter which produces edema. It is recognized that other factors may be involved in the rate of reabsorption. We emphasized that the patients studied were those who formed edema at rest, since the data were collected on resting subjects. Many patients who are compensated at rest form edema with activity. The reason for this can be ascertained only by studying patients in the exercising state. This paper is a report on the effect of exercise on the renal plasma flow and filtration rate of normal and cardiac subjects.

METHODS

Subjects were selected most of whom, at rest in the hospital, responded readily to routine therapeutic procedures. In this way it was hoped to obtain patients with relatively normal resting filtration rates. Controls consisted primarily of patients with asymptomatic neurosyphilis who were receiving penicillin therapy. Since other techniques are not suitable to demonstrate brief changes in renal plasma flow and filtration rate, the methods of Smith, Goldring and Chasis (2) were employed utilizing sodium para-amino hippurate for renal plasma flow and inulin for filtration rate.

As accurate results necessitate maintenance of a constant blood level of these materials, forms of exercise were used in which a constant intravenous infusion could be given. At first, studies were made on recumbent patients with simple alternate flexion of each leg. As it became obvious that so little exercise was insufficient, the patients were required to step up and down two steps, each 12½ inches high, approximately 40 times. These patients were relatively free of edema as a result of mercurial diuresis before exercise was undertaken. Still later, in the recumbent position, pedals were pushed which, through two single pulley arrangements, raised two 22-pound weights alternately through a distance of 8 inches. Finally, as indicated in the table, 22-pound weights were raised through a distance of 12 inches. After allowing 30 minutes to acquire a constant blood level, a 12-minute exercise period was preceded by two 15-minute control periods and followed by sometimes one, usually two, 15-minute control periods. In most cases the normal subjects were required to do more work than the cardiac subjects. All results are corrected to a body surface area of 1.73 square meters.

In L. M., a patient with constrictive pericarditis, and M. T., a patient with heart failure associated with a chest deformity, who showed reductions in filtration rate with moderate exercise, the renal sodium excretion at absolute bed rest was compared with a day of walking about the ward, sweeping, etc. The same procedure was followed in another patient, S. L. H., with constrictive pericarditis, who failed to show a reduced filtration rate with the amount of exercise given.

The filtration fraction was calculated by division of the filtration rate figure by the renal plasma flow figure. An increase above 23 to 25 per cent indicates a rise in filtration pressure, best explained by efferent arteriolar constriction (3).

RESULTS

The results obtained in the present work should be considered in relation to results previously obtained in this program of study, wherein a correlation was attempted between the actual filtration rate and the tendency of patients to form edema. Filtration rates were determined on 42 ambulatory patients, all of whom had previously been in cardiac failure and were at the time on a regimen of digitalis, low salt diet and restricted activity. Twenty-eight of them required, in ad-

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dition, the administration of mercurial diuretics once or twice a week in order to remain free of edema. The filtration rates in this group of cases are shown in Figure 1. Those who had to have diuretics are listed as "chronic," and those who did not, as "acute." It will be seen that all subjects with resting filtration rates below 80 cc. per minute required mercurial diuretics to keep them free of edema, whereas only three patients with filtration rates above 85 cc. per minute and none above 110 cc. per minute required mercurial diuretics. The amount of overlapping is surprisingly small in view of the considerable variation in activity and salt intake which undoubtedly existed. The critical level for salt retention under the conditions reported appears to be in the neighborhood of 70–80 cc. per minute.

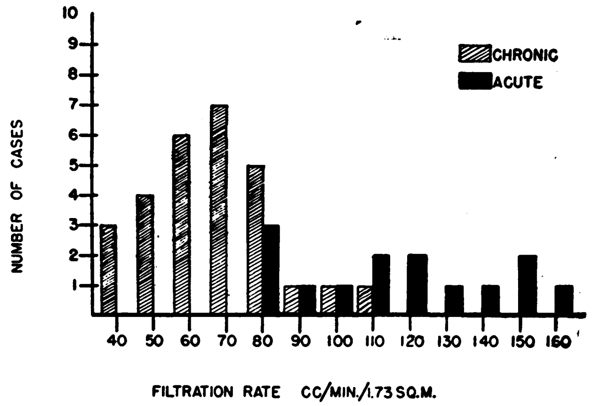

FIG. 1. FILTRATION RATES OF 42 AMBULATORY PATIENTS, PREVIOUSLY IN CARDIAC FAILURE

Those requiring diuretics listed as "chronic"; those who did not, "acute."

TABLE I

The effect of exercise on the renal plasma flow and filtration rate of normal and cardiac subjects

Patient	Diagnosis	No. complete cycles	Renal plasma flow, Before exercise	Renal plasma flow, During exercise	Renal plasma flow, After exercise	Filtration rate, Before exercise	Filtration rate, During exercise	Filtration rate, After exercise
			Ml. per 1.73 sq. m. per min. (Each figure represents a 15-minute period)					
22-lb. weight through 8 inches								
Controls								
E. J. L.	Convalescent pneumonia	100	615 482	421	405 425	125 113	114	99 106
F. W.	Meningovascular syphilis	160	530 574	570	570 568	100 103	104	104 99
Cardiacs								
L. V. E.	Syphilitic aortic insufficiency (rare diuretic required)*	183	250 232	239	239	87 94	98	93
O. P.	Syphilitic aortic insufficiency and arteriovenous aneurysm (diuretic 2 times weekly)*	160	270 260	57	233 257	73 73	16.4	74 84
22-lb. weight through 12 inches								
Controls								
R. S.	Asymptomatic neurosyphilis	150	483 490	438	423 415	128 115	108	109 110
A. G.	Asymptomatic neurosyphilis	200	367 375	336	297 298	128 127	141	130 142
G. D.	Asymptomatic neurosyphilis	295	536 483	570	475 500	122 111	127	103 113
Cardiacs								
L. B.	Hypertensive heart disease	135	215 209	51	193 197	96 88	25	108 97

TABLE I—*Continued*

Patient	Diagnosis	No.	*Ml. per 1.73 sq. m. per min.* (Each figure represents a 15-minute period)					
			Renal plasma flow			Filtration rate		
			Before exercise	During exercise	After exercise	Before exercise	During exercise	After exercise
Steps								
Controls								
F. G.	Asymptomatic neurosyphilis	80	568 518	495	539	126 123	126	127
N. D.	Asymptomatic neurosyphilis	84	408 393	264	318	119 102	91	96
D. M.	Asymptomatic neurosyphilis	88	759 755	442	820	149 152	103	182
E. C.	Asymptomatic neurosyphilis	82	405 415	306	322 350	126 117	96	111 114
R. R.	Asymptomatic neurosyphilis	88	434 448	384	452 448	103 113	107	114 106
H. D.	Asymptomatic neurosyphilis	88	724 663	436	404 760	167 161	115	103 172
Cardiacs								
M. T.	Heart failure due to chest deformity (diuretic 1 time weekly)*	62	406 384	204	448	135 131	76	159
L. M.	Constrictive pericarditis (diuretic 1 time weekly)*	80	521 370	138	412	133 95	37	114
S. L. H.	Constrictive pericarditis (no diuretic)*	84	654 676	527	502	139 147	135	129
L. V. E.	Syphilitic aortic insufficiency (rare diuretic)*	86	277 306	218	301 319	67 81	61	84 79
Horizontal leg movements								
Cardiacs								
M. B.	Hypertensive heart disease (diuretic 2 times weekly)*	100	123 98	66	131 135	69 61	31	63 60
W. F.	Rheumatic or syphilitic aortic insufficiency	100	241 233	171	307 246	85 86	58	102 86
W. R.	Syphilitic aortic insufficiency	100	280 233	258	242 258	75 73	82	79 83

* The frequency of mercurial diuretics refers to the patient in the ambulatory state. Variation in the amount of activity and variation in the salt content of the diet would probably modify this.

In reporting results with exercise, therefore, primary interest is centered on the question of whether or not the filtration rate fell below that point. In most cases the fall in filtration rate paralleled the decrease in renal plasma flow so that no comment on the latter is made in the text. Changes of less than 25 per cent are considered within the limits of technical error of the procedure.

No controls were studied using simple leg flexion in the recumbent position and the controls employing the light weights may be used for comparison. The filtration rate of one cardiac subject (W. R.) with horizontal leg flexion remained unchanged. That of another (W. F.) fell significantly but the subsequent control period level greatly exceeded the others and it is believed that the bladder may have been incompletely emptied during the exercise period, giving a false low value. A third had a resting average of 65 cc. per minute and fell to 31 cc. per minute with exercise.

Two control subjects were studied in the horizontal position with 22-pound weights moved through a distance of 8 inches. One of these showed no change and the other had a slight decrease in renal plasma flow and none in filtration rate. The renal studies of one cardiac subject were unaffected by the amount of exercise given while the other showed a striking 75 per cent reduction in plasma flow and filtration rate, the latter falling from 73 to 16 cc. per minute.

Six normal individuals were studied utilizing steps (Figure 2a and b). Each point in the figures represents the result of a 15-minute period. Two were unchanged but four had an appreciable drop in renal plasma flow during the exercise pe-

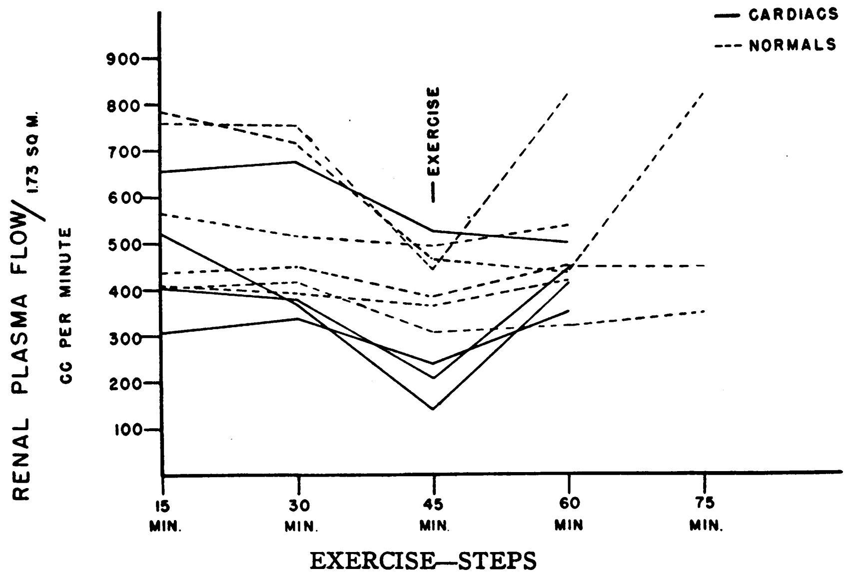

FIG. 2a. RENAL PLASMA FLOW OF 6 NORMALS AND 4 CARDIAC PATIENTS IN THE STEP EXERCISE

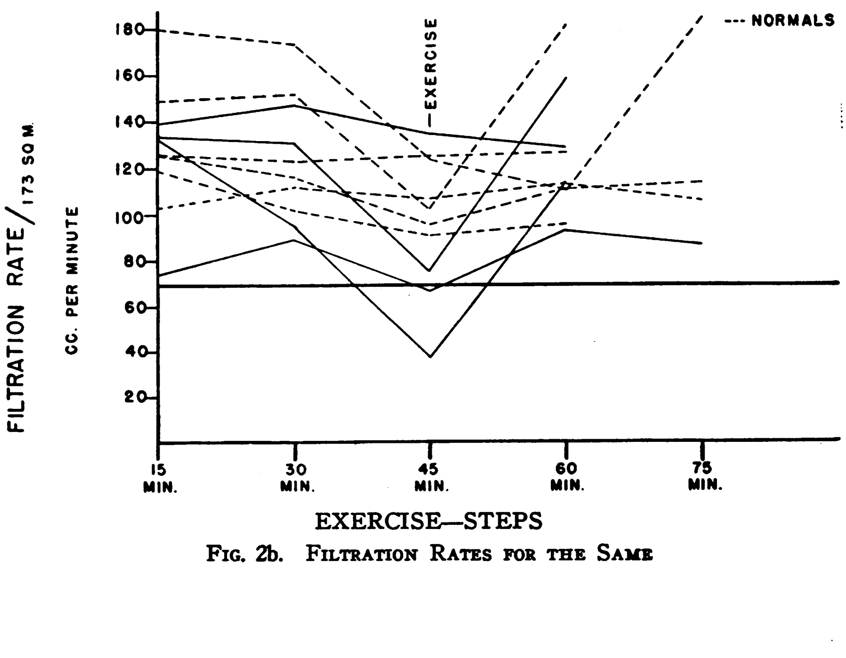

FIG. 2b. FILTRATION RATES FOR THE SAME

riod. The filtration rates also fell but none approached the critical level of 70 cc. per minute, the lowest being 91 cc. per minute. Of four patients with cardiac failure, one had no change in renal function with exercise, one had a slight decrease, one exhibited a 50 per cent drop, and one had a fall of 75 per cent. Of the last three, the first had a resting filtration rate of 74 and dropped to 61 cc. per minute. The filtration rate of the second fell from 134 to 76 cc. per minute, despite the fact that she did only 75 per cent of the required amount of exercise. The other had a marked fall from a mean of 119 to 37 cc. per minute.

Three normal individuals were able to push the 22-pound weights through a distance of 12 inches for 15 minutes without appreciable change in renal function. One did twice as much exercise as the cardiac patient. The cardiac subject had a striking decrease from 92 cc. to 25 cc. per minute.

Filtration fractions tended to rise with exercise. This was more evident in the control subjects, some of whom had rather marked drops in renal plasma flow with little change in filtration rate, suggesting efferent arteriolar constriction.

The two cardiac patients whose filtration rates fell with exercise had striking reductions in sodium output during 12 hours of walking about the ward, sweeping, etc., as compared to a 12-hour period of rest in bed. The sodium output of one fell from 104.0 mEq. to 57.4 mEq. and the other from 84.6 mEq. to 33.4 mEq. The cardiac subject who had no reduction in filtration rate with exercise had a rise in sodium output from 50.2 mEq. during a rest day to 73.4 mEq. during a day of activity. This patient had constrictive pericarditis with a venous pressure of 27 cm. of saline.

DISCUSSION

In interpreting the data presented here it must be remembered that various factors may cause an apparent absence of response of the renal blood flow to exercise, under the conditions of these methods. First, the limited amount of exercise which is possible under the experimental conditions may not tax the cardiac reserve sufficiently to produce a renal shutdown. If a patient has a normal resting renal plasma flow, as was the case with S. L. H., a fall of renal plasma flow in response to mild exercise would not be likely to occur. Marked exercise, such as running the 440-yard dash, will produce a renal shutdown even in normal individuals, as has been demonstrated by crude techniques (4). Another group of patients in which there might not be a response consists of those whose renal shutdown is already quite marked and in whom further mild stimulus might not produce a greater change. Such a case is L. V. E. However, this is not always true (see M. B.). A third group in which exercise might not be expected to lower the filtration rate is exemplified by patients with renal disease in whom salt and water retention is caused by either destruction of entire nephrons or interference with filtration by thickening of Bowman's capsule. Such a change occurs in glomerulonephritis. We have observed one such patient for a period of three years. The real test of the validity of the data is whether there is a significant reduction in the filtration rate toward the critical level for edema formation as compared to the response of the filtration rate of the normal controls. A response to light exercise in all cardiac patients selected will probably not be demonstrable until more sensitive methods of study can be applied to the selection of patients, or until we know how the renal shutdown is mediated from the stimulus of *inadequate* cardiac output. Such knowledge may bring recognition of other factors not mentioned here.

In general, patients with filtration rates below 70 cc. per minute who have normal tubular reabsorption of sodium tend to retain salt and water with an average salt intake (see "Results"). Most of the cardiac subjects in this study had resting filtration rates above 70 cc. per minute though many had a marked depression of renal plasma flow. Since the diminution in renal plasma flow and filtration rate has been shown to be related to the cardiac output (1) they must have had cardiac outputs adequate to prevent the formation of edema at rest. Even with the small amount of exercise performed in these experiments, however, many of the subjects were apparently unable to increase the cardiac output sufficiently to maintain a normal circulation in the face of the increased demands of the body. Such a situation seems to produce renal vasoconstriction (1).

The cause of the renal vasoconstriction accompanying an inadequate cardiac output is unknown. It could be a sympathetic nervous stimulation from the tissues or central nervous system. Preliminary studies in sympathectomized individuals and a patient with orthostatic hypotension indicate that this is not true (5). One would not expect a primarily renin effect in individuals with normal or elevated cardiac outputs. It could be an adrenalin effect. Stimulation from some metabolite from the tissues or some humoral substance from a specialized tissue are possibilities. Work is in progress to clarify this problem.

SUMMARY

1. Patients with heart failure who form edema at rest usually have a low resting cardiac output and a correlatively low resting renal plasma flow with a filtration rate below 70–80 cc. per minute. Since tubular reabsorption is almost complete, the low filtration of salt and water results in retention of salt and water, *i.e.,* edema. The operation of other factors in sodium reabsorption is appreciated.

2. Cardiac subjects who form edema only while exercising usually have filtration rates above 70 cc. per minute. In order to determine why they form edema it was necessary to study them under the conditions in which the edema was formed—in the exercising state.

3. With various forms of mild exercise, the filtration rates of six of 10 cardiac subjects approached or fell well below the "critical" level of 70 cc. per minute. None of the control subjects showed a comparable change in filtration rate, though a few had a definite fall in renal plasma flow.

4. Thus there seems to be a mechanism for reducing the renal plasma flow when the cardiac output is insufficient for tissue demands, perhaps in order to supply tissues such as the brain, the metabolic needs of which are greater than those of the kidney in proportion to blood supply. The possible mechanisms of this are mentioned.

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